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### **AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions and listings of claims in the application:

#### **LISTING OF CLAIMS:**

- 1. (currently amended) An IL-6 receptor IL-6 fusion protein, wherein in which said fusion protein comprises a fragment or all of the one amino acid residue constituting IL-6 receptor (SEQ ID NO:63) at the N-terminus of said fusion protein, directly linked to a fragment or all of and one amino acid residue constituting IL-6 (SEQ ID NO:64) at the C-terminus of said fusion protein are directly linked, wherein said fusion protein forms an oligomeric complex with gp130, and wherein said fusion protein induces gp130 activation.
- 2. (currently amended) An IL-6 receptor IL-6 fusion protein, wherein in which said fusion protein comprises any of amino acids 1 to 116 through any of amino acids 323 to 468 C-terminal of any one of 39 amino acid residues of from N-terminal 323th alanine residue to N-terminal 361th serine residue of the IL-6 receptor (SEQ ID NO:63) at the N-terminus of said fusion protein, is directly linked to an N-terminal amino acid residue of IL-6 (SEQ ID NO:64) at the C-terminus of said fusion protein.
- 3. (currently amended) A polynucleotide encoding an gene for coding for IL-6 receptor IL-6 fusion protein, wherein in which said fusion protein comprises a fragment or all of the one amino acid residue of IL-6R (SEQ ID NO:63) at the N-terminus of the fusion protein, directly linked to a fragment or all of and one amino acid residue of IL-6 (SEQ ID NO:64) at the

C-terminus of the fusion protein are linked directly, wherein said fusion protein forms an oligomeric complex with gp130, and wherein said fusion protein induces gp130 activation.

- 4. (currently amended) The polynucleotide gene-according to claim 3, wherein the polynucleotide encodes an gene codes for IL-6 receptor IL-6 fusion protein wherein in which said fusion protein comprises any of amino acids 1 to 116 through any of amino acids 323 to 468. C terminal of any one of 39 amino acid residues of from N terminal 323th alanine residue to N-terminal 361th serine residue of the IL-6 receptor (SEQ ID NO:63) at the N-terminus of the fusion protein, is directly linked to an N-terminal amino acid residue of IL-6 (SEQ ID NO:64) at the C-terminus of the fusion protein.
- 5. (currently amended) A yeast of *Pichia pastoris* species, wherein said yeast which is transformed by an expression vector comprising containing a polynucleotide encoding an gene for coding for IL-6 receptor IL-6 fusion protein wherein in which said fusion protein comprises a fragment or all of the one amino acid residue of IL-6 receptor (SEQ ID NO:63) at the N-terminus of the fusion protein, directly linked to a fragment or all of and one amino acid residue of IL-6 (SEQ ID NO:64) at the C-terminus of the fusion protein are linked directly, wherein said fusion protein forms an oligomeric complex with gp130, and wherein said fusion protein induces gp130 activation.
- 6. (currently amended) The yeast of *Pichia pastoris* species according to claim 5, wherein said yeast which is transformed by an expression vector comprising containing a polynucleotide encoding an gene for coding for IL-6 receptor R·IL-6 fusion protein wherein in which said fusion protein comprises any of amino acids 1 to 116 through any of amino acids 323 to 468 C-terminal of any one of 39 amino acid residues of from N-terminal 323th alanine residue

to N-terminal 361th serine residue of the IL-6 receptor (SEQ ID NO:63) at the N-terminus of the fusion protein, directly is-linked to an N-terminal amino acid residue of IL-6 (SEQ ID NO:64) at the C-terminus of the fusion protein.

- 7. (currently amended) A process for producing an IL-6 receptor IL-6 fusion protein, comprising a step of cultivating in a culture medium a yeast of a *Pichia pastoris* species having been transformed by an expression vector comprising containing a polynucleotide encoding gene for coding for an IL-6 receptor IL-6 fusion protein wherein in which said fusion protein comprises a fragment or all of the one amino acid residue of IL-6 receptor (SEQ ID NO:63) at the N-terminus of the fusion protein, directly linked to a fragment or all of and one amino acid residue of IL-6 (SEQ ID NO:64) at the C-terminus of the fusion protein are linked directly; and a step of collecting the IL-6 receptor IL-6 fusion protein as a secretory protein from the culture medium, wherein said fusion protein forms an oligomeric complex with gp130, and wherein said fusion protein induces gp130 activation.
- 8. (currently amended) TheA process for producing an IL-6 receptor IL-6 fusion protein according to claim 7, wherein said yeast is comprising a step of cultivating in a culture medium a yeast of a *Pichia pastoris* species set forth in claim 5 having been transformed by an expression vector comprising containing a polynucleotide encoding gene for coding for an IL-6 receptor IL-6 fusion protein wherein in which said fusion protein comprises any of amino acids 1 to 116 through any of amino acids 323 to 468 C terminal of any one of 39 amino acid residues of from N terminal 323th alanine residue to N terminal 361th serine residue of the IL-6 receptor (SEQ ID NO:63) at the N-terminus of the fusion protein, is directly linked to an N-terminal

amino acid residue of IL-6 (SEQ ID NO:64) at the C-terminus of the fusion protein; and a step of collecting the IL-6 receptor IL-6 fusion protein as a secretory protein from the culture medium.

9. (currently amended) A process for producing an IL-6 receptor·IL-6 fusion protein, comprising:

a step of cultivating a yeast of a *Pichia pastoris* species having been transformed by an expression vector <u>comprising containing</u> a <u>polynucleotide encoding gene for coding for</u> an IL-6 receptor IL-6 fusion protein <u>wherein in which said fusion protein comprises a fragment or all of the one amino acid residue of IL-6 receptor (SEQ ID NO:63) at the N-terminus of the fusion protein, directly linked to a fragment or all of and one amino acid residue of IL-6 (SEQ ID NO:64) at the C-terminus of the fusion protein are linked directly, in a culture medium of natural origin <u>containing comprising</u> a carbon source and no methanol,</u>

a step of and adding methanol during progress of the cultivation,

and a step of collecting the IL-6 receptor IL-6 fusion protein from the culture medium, wherein said fusion protein forms an oligomeric complex with gp130, and wherein said fusion protein induces gp130 activation.

10. (currently amended) TheA process for producing an IL-6 receptor·IL-6 fusion protein according to claim 9, wherein said yeast is comprising a step of cultivating a yeast of a Pichia pastoris species having been transformed by an expression vector comprising containing a polynucleotide encoding gene for coding for an IL-6 receptor·IL-6 fusion protein wherein in which said fusion protein comprises any of amino acids 1 to 116 through any of amino acids 323 to 468 C terminal of any one of 39 amino acid residues of from N terminal 323th alanine residue to N-terminal 361th serine residue of the IL-6 receptor (SEQ ID NO:63) at the N-terminus of the

fusion protein, directly is linked to an N-terminal amino acid residue of IL-6 (SEQ ID NO:64) at the C-terminus of the fusion protein.

- 11. (currently amended) The A process for producing an IL-6 receptor·IL-6 fusion protein according to claim 9, wherein comprising collecting the IL-6 receptor·IL-6 fusion protein is by treating a solution comprising the containing IL-6 receptor·IL-6 fusion protein with, in which one amino acid residue of IL-6 receptor (SEQ ID NO:63) and one amino acid residue of IL-6 (SEQ ID NO:64) are linked directly, by three kinds of chromatography including ion-exchange chromatography, hydrophobic chromatography, and gel-filtration chromatography to thereby collect the IL-6 receptor·IL-6 fusion protein.
- 12. (currently amended) The A-process for producing an IL-6 receptor IL-6 fusion protein according to claim 10, wherein comprising collecting the IL-6 receptor IL-6 fusion protein is by treating a solution comprising the containing IL-6 receptor IL-6 fusion protein with , in which C terminal of any one of 39 amino acid residues of from N terminal 323th alanine residue to N-terminal 361th serine residue of IL-6 receptor (SEQ ID NO:63) is linked to an N-terminal amino acid residue of IL-6 (SEQ ID NO:64), by three kinds of chromatography including ion-exchange chromatography, hydrophobic chromatography, and gel-filtration chromatography to thereby collect the IL-6 receptor IL-6 fusion protein.
  - 13-16. (canceled).
- 17. (new) An IL-6 receptor IL-6 fusion protein, wherein said fusion protein comprises a fragment or all of the IL-6 receptor (SEQ ID NO:63) at the N-terminus of said fusion protein, directly linked to any of amino acids 1 to 38 through amino acid 212 of IL-6

(SEQ ID NO:64) at the C-terminus of said fusion protein, wherein said fusion protein forms an oligomeric complex with gp130, and wherein said fusion protein induces gp130 activation.

- 18. (new) The polynucleotide according to claim 3, wherein the polynucleotide encodes an IL-6 receptor IL-6 fusion protein, wherein said fusion protein comprises a fragment or all of the IL-6 receptor (SEQ ID NO:63) at the N-terminus of the fusion protein, directly linked to any of amino acids 1 to 38 through amino acid 212 of IL-6 (SEQ ID NO:64) at the C-terminus of the fusion protein, wherein said fusion protein forms an oligomeric complex with gp130, and wherein said fusion protein induces gp130 activation.
- 19. (new) The yeast of *Pichia pastoris* species according to claim 5, wherein said yeast is transformed by an expression vector comprising a polynucleotide encoding an IL-6 receptor IL-6 fusion protein, wherein said fusion protein comprises a fragment or all of the IL-6 receptor (SEQ ID NO:63) at the N-terminus of the fusion protein, directly linked to any of amino acids 1 to 38 through amino acid 212 of IL-6 (SEQ ID NO:64) at the C-terminus of the fusion protein, wherein said fusion protein forms an oligomeric complex with gp130, and wherein said fusion protein induces gp130 activation.
- 20. (new) The process for producing an IL-6 receptor IL-6 fusion protein according to claim 7, wherein said yeast is transformed by an expression vector comprising a polynucleotide encoding an IL-6 receptor IL-6 fusion protein, wherein said fusion protein comprises a fragment or all of the IL-6 receptor (SEQ ID NO:63) at the N-terminus of the fusion protein, directly linked to any of amino acids 1 to 38 through amino acid 212 of IL-6 (SEQ ID NO:64) at the C-terminus of the fusion protein, wherein said fusion protein forms an oligomeric complex with gp130, and wherein said fusion protein induces gp130 activation.

- 21. (new) The process for producing an IL-6 receptor·IL-6 fusion protein according to claim 9, wherein said yeast is transformed by an expression vector comprising a polynucleotide encoding an IL-6 receptor·IL-6 fusion protein wherein said fusion protein comprises a fragment or all of the IL-6 receptor (SEQ ID NO:63) at the N-terminus of the fusion protein, directly linked to any of amino acids 1 to 38 through amino acid 212 of IL-6 (SEQ ID NO:64) at the C-terminus of the fusion protein, wherein said fusion protein forms an oligomeric complex with gp130, and wherein said fusion protein induces gp130 activation.
- 22. (new) The process for producing an IL-6 receptor IL-6 fusion protein according to claim 21, wherein collecting the IL-6 receptor IL-6 fusion protein is by treating a solution comprising the IL-6 receptor IL-6 fusion protein with ion-exchange chromatography, hydrophobic chromatography, and gel-filtration chromatography to thereby collect the IL-6 receptor IL-6 fusion protein.